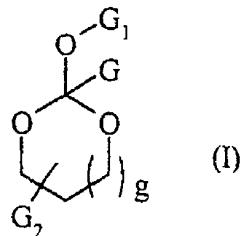


**WHAT IS CLAIMED IS:**

1. An acid-sensitive compound, or a salt thereof, comprising a cyclic ortho-ester and at least one hydrophilic substituent chosen from polyalkylene glycols, monosaccharides, polysaccharides, hydrophilic therapeutic molecules, or linear or branched alkyls,  
 5 wherein each linear or branched alkyl comprises at least 3 carbon atoms, wherein at least one of the methylene groups is optionally replaced with an amino group that is optionally substituted, and wherein at least one terminal methyl group of said linear or branched alkyl is substituted with at least one primary amine, secondary amine, tertiary amine, quaternary amine, guanidine or cyclic guanidine.

2. The acid-sensitive compound according to Claim 1, or a salt thereof, of formula (I):

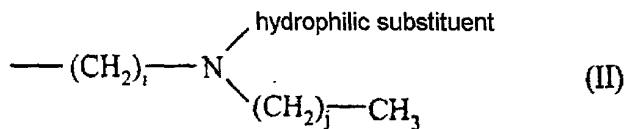


15 wherein:

- g is an integer chosen from 0, 1, 2, 3 or 4,
- G is a hydrogen atom, a straight or branched alkyl group comprising 1 to 6 carbon atoms optionally comprising at least one unsaturation, or an aryl group,,
- G<sub>1</sub> and G<sub>2</sub> is a pair of substituents chosen from one of the following substituent pairs:

(a) wherein one substituent is a hydrophilic substituent chosen from a linear or branched alkyl group comprising at least 3 carbon atoms, wherein at least one of the methylene groups is optionally replaced with an amino group that is optionally substituted, and wherein at least one terminal methyl group of said linear or branched alkyl groups are substituted with at least one primary amine, secondary amine, tertiary amine, quaternary amine, guanidine, or cyclic guanidine, and the other substituent is a hydrophobic substituent chosen from single-chain alkyls, double-chain alkyls, steroid derivatives, or hydrophobic dendrimers;

(b) or wherein one substituent is a hydrophobic linear alkyl group comprising 10 to 24 carbon atoms and optionally comprising at least one unsaturation, and the other substituent is a group of formula (II):



wherein i is an integer ranging from 1 to 4, j is an integer ranging from 9 to 23, and said hydrophilic substituent of formula (II) is a linear or branched alkyl comprising at least 3 carbon atoms, wherein at least one of the methylene groups is optionally replaced with an amino group that is optionally substituted, and wherein at least one terminal methyl group of said linear or branched alkyl is substituted with at least one primary amine, secondary amine, tertiary amine, quaternary amine, guanidine, or cyclic guanidine;

(c) or wherein one substituent is a hydrophilic polyalkylene glycol, a monosaccharide, or a polysaccharide, and the other substituent is a polyalkylene imine;

(d) or wherein one substituent is a polyalkylene glycol, monosaccharide, or polysaccharide, and the other substituent is a single-chain alkyl, double-chain alkyl,

steroid derivative, hydrophobic dendrimer, or a covalent conjugate between a single-chain alkyl, a double-chain alkyl, a steroid derivative, or a hydrophobic dendrimer and a polyalkylene glycol molecule comprising 1 to 20 monomeric units;

5 (e) or wherein one substituent is a polyalkylene glycol, a monosaccharide, or a polysaccharide, and the other substituent is a therapeutic molecule;

(f) or wherein one substituent is a hydrophilic therapeutic molecule, and the other substituent is a single-chain alkyl, a double-chain alkyl, a steroid derivative, or a hydrophobic dendrimer.

3. The acid-sensitive compound according to Claim 2, or a salt thereof, wherein G is a hydrogen atom, methyl, ethyl, or phenyl.

4. The acid-sensitive compound according to Claim 2, or a salt thereof, wherein each alkyl chain of said single-chain alkyl and said double-chain alkyl comprises 10 to 24 carbon atoms and optionally comprises at least one unsaturation.

5. The acid-sensitive compound according to Claim 2, or a salt thereof, wherein said steroid derivative is a sterol, a steroid, or a steroid hormone.

6. The acid-sensitive compound according to Claim 2, or a salt thereof, wherein said hydrophobic dendrimer is poly(benzyl ether).

7. The acid-sensitive compound according to Claim 2, or a salt thereof, wherein said polyalkylene glycol is a polyalkylene glycol having an average molecular weight ranging from  $10^2$  to  $10^5$  Daltons.

8. The acid-sensitive compound according to Claim 7, or a salt thereof, wherein said polyalkylene glycol is polyethylene glycol (PEG) having an average molecular weight ranging from  $10^2$  to  $10^5$  Daltons.

25 9. The acid-sensitive compound according to Claim 2, or a salt thereof, wherein said monosaccharide or polysaccharide is chosen from a pyranose,

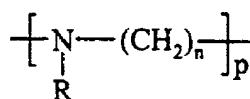
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a furanose, a dextran,  $\alpha$ -amylose, amylopectin, a fructan, a mannan, a xylan, or a arabinan.

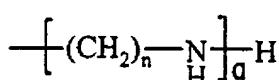
10. The acid-sensitive compound according to Claim 2, or a salt thereof, wherein said polyalkylene glycol, monosaccharide, or polysaccharide is  
5 covalently linked to a targeting element.

11. The acid-sensitive compound according to Claim 10, or a salt thereof, wherein said targeting element is a sugar, a peptide, a protein, a oligonucleotide, a lipid, a neuromediator, a hormone, a vitamin, or a derivative thereof.

10 12. The acid-sensitive compound according to Claim 2, or a salt thereof, wherein said polyalkyleneimine is a polymer comprising a monomeric units  
15 of the formula:



wherein R is a hydrogen atom or a group of the formula:



20 wherein n is an integer ranging from 2 to 10, p and q are integers chosen such that  
the sum p + q is the average molecular weight of the polymer ranges from 100 to  $10^7$   
Da,

wherein the value of n may vary between the different units -NR-(CH<sub>2</sub>)<sub>n</sub>-.

25 13. The acid-sensitive compound according to Claim 2, or a salt thereof, wherein each of the substituents G<sub>1</sub> and G<sub>2</sub> are linked to the cyclic ortho-ester via a spacer molecule.

14. The acid-sensitive compound according to Claim 13, or a salt thereof, wherein said spacer molecule is an alkyl group comprising 1 to 6 carbon atoms, a carbonyl group, an ester group, an ether group, an amide group, a carbamate group, a thiocarbamate group, a glycerol group, a urea group, a thiourea group, or a combination of said groups.

15. The acid-sensitive compound according to Claim 2, or a salt thereof, wherein said therapeutic molecule is a peptide, an oligopeptide, a protein, an antigen, an antibody to said antigen, an enzyme, an inhibitor of said enzyme, a hormone, an antibiotic, an analgesic, a bronchodilator, an antimicrobial, an antihypertensive agent, a cardiovascular agent, an agent that acts on the central nervous system, an antihistamine, an antidepressant, a tranquilizer, an anticonvulsant, an anti-inflammatory substance, a stimulant, an antiemetic agent, a diuretic agent, an antispasmodic agent, an antiischemic agent, an agent limiting cell death, or an anticancer agent.

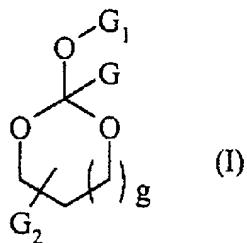
16. The acid-sensitive compound according to Claim 2, or a salt thereof, wherein said linear or branched alkyl comprises at least 3 carbon atoms, wherein at least one of the methylene groups is optionally replaced with an amino group that is substituted with a methyl group.

17. A composition comprising at least one acid-sensitive compound, or a salt thereof, comprising a cyclic ortho-ester and at least one hydrophilic substituent chosen from polyalkylene glycols, monosaccharides, polysaccharides, hydrophilic therapeutic molecules, or linear or branched alkyls, wherein each linear or branched alkyl comprises at least 3 carbon atoms, wherein at least one of the methylene groups is optionally replaced with an amino group that is optionally substituted, and wherein at least one terminal methyl group of said linear or branched alkyl is substituted with at least one primary amine, secondary amine,

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tertiary amine, quaternary amine, guanidine or cyclic guanidine.

18. The composition according to Claim 17, comprising at least one acid-sensitive compound of formula (I):

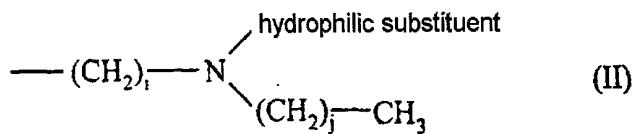


or a salt thereof,

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wherein:

- $g$  is an integer chosen from 0, 1, 2, 3 or 4,
- $G$  is a hydrogen atom, a straight or branched alkyl group comprising 1 to 6 carbon atoms optionally comprising at least one unsaturation, or an aryl group,
- $G_1$  and  $G_2$  is a pair of substituents chosen from one of the following substituent pairs:
  - (a) wherein one substituent is a hydrophilic substituent chosen from a linear or branched alkyl group comprising at least 3 carbon atoms, wherein at least one of the methylene groups is optionally replaced with an amino group that is optionally substituted, and wherein at least one terminal methyl group of said linear or branched alkyl groups are substituted with at least one primary amine, secondary amine, tertiary amine, quaternary amine, guanidine, or cyclic guanidine, and the other substituent is a hydrophobic substituent chosen from single-chain alkyls, double-chain alkyls, steroid derivatives, or hydrophobic dendrimers;
  - (b) or wherein one substituent is a hydrophobic linear alkyl group comprising 10 to 24 carbon atoms and optionally comprising at least one unsaturation, and the other substituent is a group of formula (II):



wherein i is an integer ranging from 1 to 4, j is an integer ranging from 9 to 23, and said hydrophilic substituent of formula (II) is a linear or branched alkyl comprising at least 3 carbon atoms, wherein at least one of the methylene groups is optionally replaced with an amino group that is optionally substituted, and wherein at least one terminal methyl group of said linear or branched alkyl is substituted with at least one primary amine, secondary amine, tertiary amine, quaternary amine, guanidine, or cyclic guanidine;

- (c) or wherein one substituent is a hydrophilic polyalkylene glycol, a monosaccharide, or a polysaccharide, and the other substituent is a polyalkylene imine;
- (d) or wherein one substituent is a polyalkylene glycol, monosaccharide, or polysaccharide, and the other substituent is a single-chain alkyl, double-chain alkyl, steroid derivative, hydrophobic dendrimer, or a covalent conjugate between a single-chain alkyl, a double-chain alkyl, a steroid derivative, or a hydrophobic dendrimer and a polyalkylene glycol molecule comprising 1 to 20 monomeric units;
- (e) or wherein one substituent is a polyalkylene glycol, a monosaccharide, or a polysaccharide, and the other substituent is a therapeutic molecule;
- (f) or wherein one substituent is a hydrophilic therapeutic molecule, and the other substituent is a single-chain alkyl, a double-chain alkyl, a steroid derivative, or a hydrophobic dendrimers.

19. The composition according to claim 18, wherein G<sub>1</sub> and G<sub>2</sub> of said acid-sensitive compound are defined as in said substituent pairs (a), (b), (c) or

(d); and wherein said composition further comprises at least one biologically active substance.

20. The composition according to Claim 19, wherein said biologically active substance is a nucleic acid, a peptide, an oligopeptide, a protein, an antigen, an antibody to said antigen, an enzyme, an inhibitor of said enzyme, a hormone, an antibiotic, an analgesic, a bronchodilator, an antimicrobial, an antihypertensive agent, a cardiovascular agent, an agent that acts on the central nervous system, an antihistamine, an antidepressant, a tranquilizer, an anticonvulsant, an anti-inflammatory substance, a stimulant, an antiemetic agent, a diuretic agent, an antispasmodic agent, an antiischemic agent, an agent limiting cell death, or an anticancer agent.

21. The composition according to Claim 17, further comprising at least one adjuvant.

22. The compositions according to Claim 21, wherein said adjuvant comprises at least one neutral lipid.

23. The composition according to Claim 22, wherein said adjuvant comprises at least one neutral lipid chosen from natural zwitterionic lipids, synthetic zwitterionic lipids, and lipids lacking an ionic charge under physiological conditions.

24. The composition according to Claim 23, wherein said adjuvant comprises at least one neutral lipid chosen from dioleoylphosphatidylethanolamine (DOPE), oleoyl-palmitoylphosphatidylethanolamine (POPE), distearoyl-phosphatidylethanolamine (DSPE), dipalmitoylphosphatidyl-ethanolamine (DPPE), dimirystoylphosphatidylethanolamine (DMPE), DOPE N-methylated 1 to 3 times, POPE N-methylated 1 to 3 times, DSPE N-methylated 1 to 3 times, DPPE N-methylated 1 to 3 times, phosphatidylglycerols, diacylglycerols, glycosyldiacylglycerols, cerebrosides, sphingolipids, and asialogangliosides.

25. The composition according to Claim 24, wherein said adjuvant comprises at least one cerebroside chosen from galactocerebrosides.

26. The composition according to Claim 24, wherein said adjuvant comprises at least one sphingolipid chosen from sphingomyelins,

5 27. The composition according to Claim 24, wherein said adjuvant comprises at least one asialogangliosides chosen from asialoGM1 and asialoGM2.

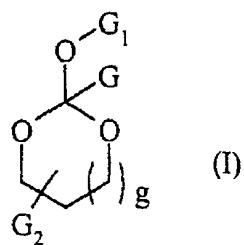
28. The composition according to Claim 17, further comprising a pharmaceutically acceptable vehicle for an injectable formulation.

10 29. The composition according to Claim 17, further comprising a pharmaceutically acceptable vehicle for administration to skin or mucous membranes.

15 30. A method for treating a disease or disorder comprising administering at least one acid-sensitive compound, or a salt thereof, comprising a cyclic ortho-ester and at least one hydrophilic substituent chosen from polyalkylene glycols, monosaccharides, polysaccharides, hydrophilic therapeutic molecules, or linear or branched alkyls,

20 wherein each linear or branched alkyl comprises at least 3 carbon atoms, wherein at least one of the methylene groups is optionally replaced with an amino group that is optionally substituted, and wherein at least one terminal methyl group of said linear or branched alkyl is substituted with at least one primary amine, secondary amine, tertiary amine, quaternary amine, guanidine or cyclic guanidine.

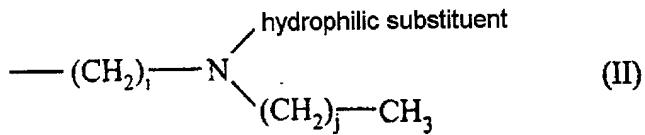
31. The method according to Claim 30, comprising administering at least one acid-sensitive compound of formula (I):



or a salt thereof,

wherein:

- g is an integer chosen from 0, 1, 2, 3 or 4,
- G is a hydrogen atom, a straight or branched alkyl group comprising 1 to 6 carbon atoms optionally comprising at least one unsaturation, or an aryl group,
- G<sub>1</sub> and G<sub>2</sub> is a pair of substituents chosen from one of the following substituent pairs:
  - (a) wherein one substituent is a hydrophilic substituent chosen from a linear or branched alkyl group comprising at least 3 carbon atoms, wherein at least one of the methylene groups is optionally replaced with an amino group that is optionally substituted, and wherein at least one terminal methyl group of said linear or branched alkyl groups are substituted with at least one primary amine, secondary amine, tertiary amine, quaternary amine, guanidine, or cyclic guanidine, and the other substituent is a hydrophobic substituent chosen from single-chain alkyls, double-chain alkyls, steroid derivatives, or hydrophobic dendrimers;
  - (b) or wherein one substituent is a hydrophobic linear alkyl group comprising 10 to 24 carbon atoms and optionally comprising at least one unsaturation, and the other substituent is a group of formula (II):



wherein i is an integer ranging from 1 to 4, j is an integer ranging from 9 to 23, and said hydrophilic substituent of formula (II) is a linear or branched alkyl comprising at least 3 carbon atoms, wherein at least one of the methylene groups is optionally replaced with an amino group that is optionally substituted, and wherein at least one terminal methyl group of said linear or branched alkyl is substituted with at least one primary amine, secondary amine, tertiary amine, quaternary amine, guanidine, or cyclic guanidine;

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- (c) or wherein one substituent is a hydrophilic polyalkylene glycol, a monosaccharide, or a polysaccharide, and the other substituent is a polyalkylene imine;
- (d) or wherein one substituent is a polyalkylene glycol, monosaccharide, or polysaccharide, and the other substituent is a single-chain alkyl, double-chain alkyl, steroid derivative, hydrophobic dendrimer, or a covalent conjugate between a single-chain alkyl, a double-chain alkyl, a steroid derivative, or a hydrophobic dendrimer and a polyalkylene glycol molecule comprising 1 to 20 monomeric units;
- (e) or wherein one substituent is a polyalkylene glycol, a monosaccharide, or a polysaccharide, and the other substituent is a therapeutic molecule;
- (f) or wherein one substituent is a hydrophilic therapeutic molecule, and the other substituent is a single-chain alkyl, a double-chain alkyl, a steroid derivative, or a hydrophobic dendrimer.

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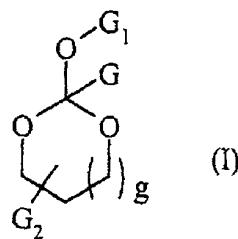
32. The method according to Claim 31, wherein said G<sub>1</sub> and G<sub>2</sub> are defined as in said substituent pairs (a), (b), (c) or (d); and wherein said method further comprises transfection of nucleic acids.

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33. The method according to Claim 31, wherein said wherein  $G_1$  and  $G_2$  are defined as in said substituent pairs (e) or (f).

34. A method for transfecting a nucleic acid comprising at least one acid-sensitive compound, or a salt thereof, comprising a cyclic ortho-ester and at least one hydrophilic substituent chosen from polyalkylene glycols, monosaccharides, polysaccharides, hydrophilic therapeutic molecules, or linear or branched alkyls, wherein each linear or branched alkyl comprises at least 3 carbon atoms, wherein at least one of the methylene groups is optionally replaced with an amino group that is optionally substituted, and wherein at least one terminal methyl group of said linear or branched alkyl is substituted with at least one primary amine; secondary amine, tertiary amine, quaternary amine, guanidine or cyclic guanidine.

35. The method according to Claim 34, comprising at least one acid-sensitive compound of formula (I):



or a salt thereof,

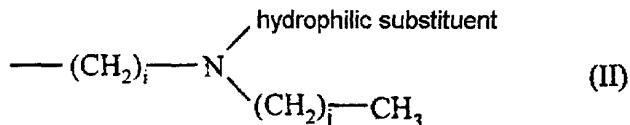
wherein:

- $g$  is an integer chosen from 0, 1, 2, 3 or 4,
- $G$  is a hydrogen atom, a straight or branched alkyl group comprising 1 to 6 carbon atoms optionally comprising at least one unsaturation, or an aryl group,
- $G_1$  and  $G_2$  is a pair of substituents chosen from one of the following substituent pairs:

(a) wherein one substituent is a hydrophilic substituent chosen from a linear or

branched alkyl group comprising at least 3 carbon atoms, wherein at least one of the methylene groups is optionally replaced with an amino group that is optionally substituted, and wherein at least one terminal methyl group of said linear or branched alkyl groups are substituted with at least one primary amine, secondary amine, tertiary amine, quaternary amine, guanidine, or cyclic guanidine, and the other substituent is a hydrophobic substituent chosen from single-chain alkyls, double-chain alkyls, steroid derivatives, or hydrophobic dendrimers;

(b) or wherein one substituent is a hydrophobic linear alkyl group comprising 10 to 24 carbon atoms and optionally comprising at least one unsaturations, and the other substituent is a group of formula (II):



wherein i is an integer ranging from 1 to 4, j is an integer ranging from 9 to 23, and said hydrophilic substituent of formula (II) is a linear or branched alkyl comprising at least 3 carbon atoms, wherein at least one of the methylene groups is optionally replaced with an amino group that is optionally substituted, and wherein at least one terminal methyl group of said linear or branched alkyl is substituted with at least one primary amine, secondary amine, tertiary amine, quaternary amine, guanidine, or cyclic guanidine;

- (c) or wherein one substituent is a hydrophilic polyalkylene glycol, a monosaccharide, or a polysaccharide, and the other substituent is a polyalkylene imine;
- (d) or wherein one substituent is a polyalkylene glycol, monosaccharide, or polysaccharide, and the other substituent is a single-chain alkyl, double-chain alkyl, steroid derivative, hydrophobic dendrimer, or a covalent conjugate between a single-

chain alkyl, a double-chain alkyl, a steroid derivative, or a hydrophobic dendrimer and a polyalkylene glycol molecule comprising 1 to 20 monomeric units;

(e) or wherein one substituent is a polyalkylene glycol, a monosaccharide, or a polysaccharide, and the other substituent is a therapeutic molecule;

5 (f) or wherein one substituent is a hydrophilic therapeutic molecule, and the other substituent is a single-chain alkyl, a double-chain alkyl, a steroid derivative, or a hydrophobic dendrimers.

36. The method according to Claim 34, comprising transfecting a nucleic acid into at least one cell.

40 37. The method according to Claim 35, wherein said  $G_1$  and  $G_2$  are defined as in said substituent pairs (a), (b), (c) or (d).

38. The method according to claim 35, wherein said  $G_1$  and  $G_2$  are defined as in said substituent pairs (e) or (f).

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